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**Serial No. 10/817,036**

**PATENT**

**REMARKS**

Upon entry of this response, claims 1-22 will be pending in this application. Independent claims 1, 5, 6, 8 and 15 have been amended to clarify that the claimed invention is related to melanin related affliction, skin pigmentation, hair color and hair removal. Support for the amended independent claims are fully supported by the specification at, for example, page 40-44 (Examples 1-8, where in each case the medical provider identifies the patient with a particular condition that can be treated by the administration of a botulinum toxin). Amended claim 2 is fully supported by the specification at, for example, page 43 (Example 6) and page 41-42 (Examples 2-5). Amended claim 7 and new claim 16 are fully supported by the specification at, for example, page 41 (Example 3). Amended claims 9 and 10 are fully supported by the specification at, for example, page 43 (Example 7). New claim 17 is fully supported by the specification at, for example, page 21, lines 11-24, and page 40 (Example 1). New claims 18-21 are fully supported by the specification at, for example, page 21, lines 11-24 and the original claims 2-4.

New claim 22 recites that the botulinum toxin is native. A native botulinum toxin is not a chimera, e.g., a botulinum toxin that is attached a targeting moiety. Support for new claim 22 is fully supported by the specification at, for example, the paragraph bridging page 22 and 23.

No new matter is added.

**The Claims Satisfy §112 Requirements**

Claims 3, 4, 7 and 10 have been rejected under 35 U.S.C. §112, second paragraph, for allegedly reciting features that lack antecedent basis.

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With regard to claims 3 and 4, the Office Action alleges that the step of increasing or decreasing pigmentation does not find antecedent basis in claim 2. Although Applicant respectfully disagrees, Applicant has amended claim 2 to explicitly recite that the method of treating a pigmentation disorder may be by administering a botulinum toxin to increase or decrease the pigmentation of the skin. Thus, every feature of claims 3 and 4 has a proper antecedent basis.

With regard to claim 7, the Office Action alleges that the terms "size", "reducing" and "influenced" lack antecedent basis from claim 1. Claim 7 has been amended and new claim 16 has been added to clarify the antecedent basis for the terms at issue. Thus, every feature of claim 7 has a proper antecedent basis.

With regard to claim 10, the Office Action alleges that the terms "decreasing" and "hair color" lack antecedent basis from claim 1. Claim 10 has been amended to clarify the antecedent basis for the terms at issue. Thus, every feature of claim 10 has a proper antecedent basis.

### **The Claims Are Novel**

It is important that the Office recognize that a reference can only anticipate (explicitly or inherently) the claims if the reference discloses *all* of the features of the claims (explicitly or inherently). With regard to the requirements to establish inherent anticipation, the MPEP at 2112 IV states that:

To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

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(emphasis added). As will be detailed below, none of the references anticipates the claimed invention because none of the references discloses (explicitly or inherently) ALL the steps of the claims.

### **The Vazquez Reference**

Claims 1-6 and 11-14 are rejected under 35 U.S.C. §102(b) for allegedly being anticipated by Vazquez et al. (Actu Derm Venereol, 2002, 82(2): 154-156, hereinafter “the Vazquez reference”). Contrary to the Office Action’s allegation, the Vazquez reference cannot anticipate the claimed invention because it does not disclose all the features of the claimed invention. For example, claim 1 recites a method comprising the step of “identifying a patient in need of treatment for a melanin related affliction, where the affliction can be treated by an administration of a botulinum toxin”. The Vazquez reference does not disclose this step (or the step of identifying a patient in need of influencing skin pigmentation (claim 5)).

Instead, the Vazquez reference discloses a method of treating “eccrine naevus”, which is a localized hyperhidrosis, by administering a botulinum toxin to the skin area (the Vazquez reference, page 154, first column). Although the Vazquez reference discloses that a slight hyperpigmentation occasionally accompanies an eccrine naevus, it is important to recognize that the Vazquez reference does not disclose that the administration of a botulinum toxin affects the hyperpigmentation in any way. The reference only discloses that the administration of a botulinum toxin reduces the hyperhidrosis (the Vazquez reference, paragraph bridging pages 154 and 155). Thus, at most the Vazquez reference discloses a method of identifying a patient with hyperhidrosis, which can be treated with the administration of a botulinum toxin. Thus, it is clear that the Vazquez reference does not disclose the step of “identifying a patient in need of treatment for a melanin related affliction, where the affliction can be treated by an administration of a botulinum toxin” of claim 1.

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Further, the step of identifying a patient in need of (a) treatment for a melanin related affliction that can be treated by an administration of a botulinum toxin (independent claims 1 and 6) or (b) influencing skin pigmentation that can be influenced by the administration of a botulinum toxin (claim 5) is not necessarily present in the disclosure of the Vazquez reference. For example, the medical provider in the Vazquez reference did not identify a patient in need of treatment for a hyperpigmentation that can be treated by an administration of a botulinum toxin. The medical provider in the Vazquez reference only identified a patient in need of treatment of a hyperhidrosis that can be treated by the administration of a botulinum toxin. Further, as mentioned above, the Vazquez reference does not disclose whether the administration of botulinum toxin has any affect on the hyperpigmentation at all. Thus, the Vazquez reference cannot inherently anticipate the claims.

### **The Maurer Reference**

Claims 8-9 and 15 are rejected under 35 U.S.C. §102(b) for allegedly being inherently anticipated by PG-Pub 2002/0028765 A1 (hereinafter "the Maurer reference"). Contrary to the Office Action's allegation, the Maurer reference does not inherently anticipate the claims because the reference does not explicitly or inherently disclose all the features of the claims. For example, the claims recite a method comprising the step of identifying a patient in need of altering hair color where an administration of a botulinum toxin can alter the color (independent claim 8), or a patient in need of hair removal wherein an administration of a botulinum toxin can remove the hair (independent claim 15).

These steps are not explicitly disclosed by the Maurer reference. The Maurer reference discloses a method for inducing hair growth (not hair removal as presently claimed) by administering a botulinum toxin to the head. As such, the Maurer reference discloses a step of identifying a patient in need of hair growth. However, the reference

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does not explicitly disclose a step of identifying a patient in need of (a) altering hair color where an administration of a botulinum toxin can alter the color, or (b) a patient in need of hair removal wherein an administration of a botulinum toxin can remove the hair.

The Maurer reference also does not inherently disclose the steps at issue, because these steps are **not necessarily present from the disclosure of the Maurer reference**. For example, the step of identifying a patient in need of hair growth in the Maurer reference has nothing to do with the step of identifying a patient in need of (a) altering hair color where an administration of a botulinum toxin can alter the color, or (b) a patient in need of hair removal wherein an administration of a botulinum toxin can remove the hair. Thus, the Vazquez reference cannot inherently anticipate the claims

### **The Waugh Reference**

Claims 1-6 and 8-14 are rejected under 35 U.S.C. §102(e) for allegedly being anticipated by US PG-Pub 2004/0220100 A1 (hereinafter “the Waugh reference”). Contrary to the Office Action’s allegation, the Waugh reference cannot anticipate the claimed invention because it does not disclose all the features. For example, claim 1 recites a method comprising the step of “identifying a patient in need of treatment for a melanin related affliction, where the affliction can be treated by an administration of a botulinum toxin”. The Waugh reference does not disclose this step. Instead, the Waugh reference discloses methods for transdermal delivery of biologically active agents (e.g., botulinum toxin), where the methods comprise the step of topically applying the agent to the skin of a patient. There is nothing in the disclosure of the Waugh reference that teaches that the step of topically applying the agent to the skin of a patient can treat a melanin related affliction. Thus, the claims are novel over the Waugh reference.

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### The Pastan Reference

Claims 1-6 and 8-14 are rejected under 35 U.S.C. §102(e) for allegedly being anticipated by US PG-Pub 2004/0087772 A1 (hereinafter "the Pastan reference").

As a preliminary matter, the Pastan reference cannot anticipate new claim 22 because the claim recites the use of a native (i.e., non-chimeric) botulinum toxin, whereas the Pastan reference only teaches the use of chimeric botulinum toxin.

With regards to the claims presently being rejected, it is important to understand that a reference can only anticipate a claimed method if it is fully enabling. *Bristol-Myers Squibb v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1374 (Fed. Cir. 2001). The Pastan reference cannot anticipate the claimed invention because it is *non-enabling with respect to methods for treating melanin related afflictions*.

The Pastan reference discloses that the XAGE-1 protein is found in various cancerous cells, such as melanoma cells. The Pastan reference further discloses that a botulinum toxin attached to an anti-XAGE-1 protein can direct the botulinum toxin to the melanoma cell and kill the cell (the Pastan reference, paragraph [0189]). Although the Pastan reference mentions that it is possible to administer a botulinum-toxin/anti-XAGE-1 chimera to treat melanoma, the disclosure is actually non-enabling. For example, the Pastan reference *does not* teach the appropriate dose of the chimera to administer to treat the melanoma, as does the present specification at page 41-42, Example 4, where the dose of the botulinum toxin is properly taught so that one of ordinary skill would know how to practice the presently claimed invention. Without knowing the appropriate dose of the chimera to administer from the Pastan reference, one of ordinary skill would not know how to use the chimera as taught by the Pastan reference to treat a melanoma. Thus, the Pastan reference is non-enabling with respect to the method of treating melanoma with a botulinum toxin.

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As the Pastan reference is non-enabling with respect to the method of administering a botulinum toxin to treat melanoma, it cannot anticipate the claimed invention. Thus, the claimed invention is novel over the Pastan reference.

New claims 18-21 are directed to a method of treating a melanin related affliction, where the affliction is not a melanoma. Thus, claims 18-21 are clearly novel over the Pastan reference.

In view of the foregoing, Applicant submits that the pending claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,



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